IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF APPEALS AND PATENT INTERFERENCES

In re Application of:	)	
	)	
Wood *et al.*	)	
	)	
Serial No.: 09/577,489	)	Group Art Unit: 1616
	)	
Filed: May 25, 2000	)	Examiner: Sabiha N. Qazi
	)	
For: ***METHODS OF ADMINISTERING LIQUID DROPLET AEROSOLS OF NANOPARTICULATE DRUGS***	)	

APPEAL BRIEF

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Sir:

This Appeal Brief is being filed with a check in the amount of $500.00 covering the appeal fee. If this fee is deemed insufficient, Appellants authorize charging any deficiency (as well as crediting any balance) to deposit account 19-0741.

This is an appeal from a final Office Action dated June 17, 2004, and the Advisory Action dated August 18, 2004, finally rejecting claims 28-40, 42-45 and 47-59 under 35 U.S.C. § 103(a) over John S. James, *Aerosol Pentamidine Gets 'Treatment IND' Approval*, AIDS TREATMENT NETWORK ARTICLE, No. 74 (February 10, 1989) ("James"), in view of Liversidge *et al.*, U.S. Patent No. 5,145,684 ("Liversidge "). These claims were also rejected under 35 U.S.C. § 103(a) over Wiedmann *et al.*, U.S. Patent No. 5,747,001 ("Wiedmann")in view of Wood *et al.*, U.S. Patent No. 6,264,922 ("Wood") and Liversidge.

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I. REAL PARTY IN INTEREST

The real party in interest is the assignee, ELAN PHARMA INTERNATIONAL LIMITED, Wil House, Shannon Business Park, Shannon, Co. Clare, Ireland.

II. RELATED APPEALS AND INTERFERENCES

None of the appellants, appellants' legal representative, or their assignee is aware of any related appeals or interferences that will affect directly or be affected directly by or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF CLAIMS

All pending claims, i.e., claims 28-40, 42-45 and 47-49, are on appeal and are attached hereto in APPENDIX A.

IV. STATUS OF AMENDMENTS

In response to a non-final Office Action dated January 21, 2004, claims 28, 39, and 40 were amended, new claims 47-59 were added, and claims 10-27, 41 and 46 were canceled. Pending claims 28-40, 42-45 and 47-59 were deemed pending in a final Office Action dated June 17, 2004.

In a reply dated July 22, 2004 to the final Office Action, the claims were not amended. An Advisory Action that issued on August 18, 2004 indicated that the July 22nd response was entered but did not place the application in condition for allowance.

V. SUMMARY OF THE CLAIMED INVENTION

Independent claim 28 is involved in this appeal. This claim relates to a method of delivering to the lungs of a mammal an aerosol formulation of a crystalline particles of a therapeutic agent that is poorly soluble in water. The aerosol composition comprises aqueous droplets that are less than about fifty microns (50000 nm) in diameter. The aqueous droplets themselves comprise water, a therapeutic nanoparticulate agent, and at least one surface modifier. The nanoparticulate active agent particles have a submicron particle size and the at

least one surface modifier adsorbs to the surface of the active agent particles. Support for claim 28 can be found on pages 2-3 of the specification.

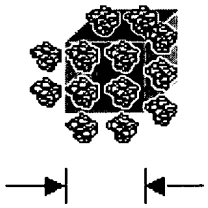
Applicants present the following chart showing explicit support in the '103 application for the independent claim 28:

Claim 28	Exemplary Support in the Application
28. A method of delivering an aerosol to the lungs of a mammal comprising the steps of:	"In yet another aspect of the invention, there is provided a method of treating a mammal comprising the steps of: . . . b) administering said aerosol to the respiratory system of said mammal." (Page 2, line 35, through page 3, line 5)
(a) providing an aerosol composition, wherein said composition comprises aqueous droplets	"there is provided a method of treating a mammal comprising the steps of: a) forming an aerosol of an aqueous dispersion . . ." (Page 2, line 35, through page 3, line 1.)
having a particle size of less than about fifty microns in diameter,	"The droplets in the aerosols typically have a size less than about 50 microns in diameter . . ." (Page 3, lines 18-19.)
wherein the aqueous droplets comprise: (i) water,	"there is provided a method of treating a mammal comprising the steps of: a) forming an aerosol of an aqueous dispersion of nanoparticles,
(ii) crystalline particles of a therapeutic agent	"there is provided a method of treating a mammal comprising the steps of: a) forming an aerosol of an aqueous dispersion of nanoparticles, said nanoparticles comprising insoluble therapeutic agent particles . . ." (Page 2, line 35, through page 3, line 2.) "The therapeutic or diagnostic agent exists as a discrete, crystalline phase." (Page 4, lines 11-12.)
which is poorly soluble in water,	"The therapeutic or diagnostic agent must be poorly soluble and dispersible in at least one liquid medium. . . A preferred liquid dispersion medium is water." (Page 4, lines 17-21.)
wherein the crystalline particles have a submicron particle size; and	In a particularly preferred method, a therapeutic or diagnostic agent is prepared in

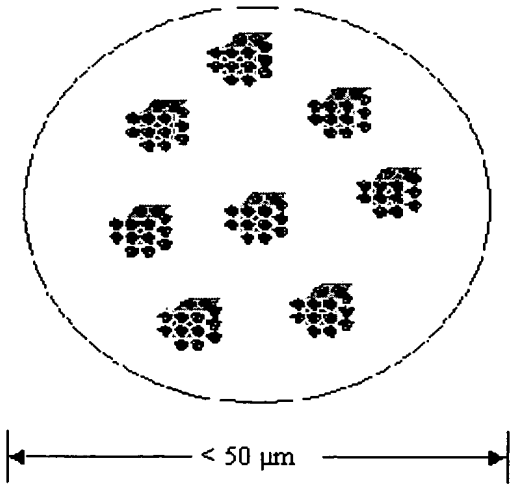
Claim 28	Exemplary Support in the Application
	the form of submicron particles . . . (Page 13, lines 14-15.) "The coarse therapeutic or diagnostic agent selected can then be added to a liquid medium in which it is essentially insoluble to form a premix. . . .The premix can be used directly by subjecting it to mechanical means to reduce the average particle size in the dispersion to less than 1000 nm." (Page 10, lines 14-25.) "As used herein, particle size refers to a number average particle size as measured by conventional particle size measuring techniques well known to those skilled in the art . . . By "an effective average particle size of less than about 1000 nm . . . (Page 16, lines 19-25.)
(iii) at least one surface modifier adsorbed on the surface of the crystalline therapeutic agent particles; and	having a surface modifier on the surface thereof; (Page 3, line 3.)
(b) administering said aerosol composition to the respiratory system of said mammal.	b) administering said aerosol to the respiratory system of said mammal. (Page 3, lines 4-5.)

The claimed invention is directed to a method of delivering to the lungs of a mammal an aerosol formulation of a poorly water-soluble nanoparticulate therapeutic agent. Prior to the claimed invention, delivery of poorly water-soluble active agents to the lung was extremely inefficient. *See* specification at page 1, lines 12-14. For example, using conventional processes it is estimated that only about 10 to 20% of an active agent reaches the lung because of losses to the device used to deliver the agent, loss to the mouth and throat, and loss due to exhalation. *See* specification at page 1, lines 17-20. Such losses lead to undesirable variable therapeutic agent levels and poor therapeutic control. *See* specification at page 1, lines 20-21. Moreover, deposition of the agent to the mouth and throat can lead to systemic absorption and undesirable side effects. *See* page 1, lines 21-22, of the application.

The method of the invention comprises administering an aerosol composition which comprises aqueous droplets that are less than about fifty microns (50,000 nm) in diameter. The aqueous droplets comprise: (i) water, (ii) a therapeutic nanoparticulate agent, and (iii) at least one surface modifier. The nanoparticulate active agent particles have an average diameter of 1000 nm or less and one or more surface modifiers adsorbed to the surface of the active agent particles, as shown below:



The nanoparticulate active agent particles, having surface modifier adsorbed to the surface thereof, are dispersed in water An exemplary aqueous droplet of an aerosol containing nanoparticulate active agent particles, with a surface modifier adsorbed to the surface of the agent particles, is graphically represented below:



Prior to the claimed invention, nanoparticulate poorly water-soluble active agent formulations were known. *See e.g.*, U.S. Patent No. 5,145,684, cited by the examiner. It was not known, however, that such nanoparticulate active agent compositions could be prepared in an aerosol formulation.

The claimed invention satisfies a need in the art for aerosol compositions that can deliver a poorly water-soluble active agent to the lungs, a need which is not met by prior disclosures. Moreover, the claimed invention is not described or suggested in the cited prior art.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The examiner maintained a rejection of claims 28-40, 42-45 and 47-59 under 35 U.S.C. § 103(a) as being allegedly obvious over James and Liversidge.

The examiner also maintained a rejection of claims 28-40, 42-45 and 47-59 under 35 U.S.C. § 103(a) as allegedly being obvious over Wiedmann, Wood and Liversidge.

VII. ARGUMENTS

A. Rejection of Claims 28-40, 42-45 and 47-59 Under 35 U.S.C. § 103(a) over James and Liversidge

To establish a *prima facie* case of obviousness under 35 U.S.C. § 103(a), the examiner must show: (1) at least a suggestion in the prior art of each element recited in the claim at issue, (2) some suggestion or motivation to have combined those elements, as proposed by the examiner, and (3) a reasonable expectation of success, likewise evidenced in the prior art, for the proposed combination. Furthermore, the Examiner must ascertain that the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made. As described below, the Examiner has not met this burden.

Claims 28-40, 42-45 and 47-59 were rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over James in view of Liversidge.

1. Examiner's Basis for the Obviousness Rejection

In support of this ground for rejection, the Examiner stated that "it would have been obvious for one of skill in the art at the time of the invention . . . to prepare an aerosol composition to use for the treatment of respiratory diseases because Liversidge et al. teaches

the average particle size, surface modifier, and all other limitations of the presently claimed invention EXCEPT for aerosols." Office Action dated June 17, 2004 at 4.

2. Because James is Directed to Compositions of *Water-Soluble* Active Agents, James and Liversidge Do Not Provide A Motivation To Prepare an Aerosol Formulation of a Poorly Water-Soluble Nanoparticulate Agent With a Reasonable Expectation of Success

James describes *water-soluble* pentamidine aerosols used for the prevention of pneumocystitis. James does not teach or suggest aerosols comprising *poorly water-soluble* active agents, nor does James teach aerosols comprising crystalline nanoparticulate active agents.

Liversidge is directed to compositions comprising a nanoparticulate active agent having a particle size of less than about 400 nm, and a surface stabilizer adsorbed onto the surface of the active agent. *See* Liversidge at col. 2, lines 38-43. Liversidge does not teach or suggest aerosol formulations of such compositions, or methods of administering aerosol formulations of such compositions.

Because James is directed to *water-soluble* active agents, there is no motivation to combine the teaching of Liversidge and James to obtain the claimed method.

3. Prior Art Teaches *Away* from the Combination of James and Liversidge, as the Prior Art Teaches that Aerosols of Poorly Water-Soluble Active Agents are Ineffective

The examiner has failed to meet her burden of establishing a *prima facie* case of obviousness because she has merely combined the James and Liversidge references, without providing a motivation to do so. In fact, a skilled artisan would *not* be motivated to merge the teachings in the cited publications to obtain an aerosol of a poorly water-soluble nanoparticulate agent, as is presently claimed, with a reasonable expectation of success. Neither James nor Liversidge, either explicitly or implicitly, support this combination. Thus, the subject matter ***as a whole*** is not obvious.

Specifically, the Examiner did not consider the totality of the evidence in maintaining the obviousness rejection, such as the prior art references cited by appellants during

prosecution: Cameron *et al.*, *Crit. Care Med.*, 18(8):866-870 (1990) ("Cameron"); Nikander *et al., J. Aerosol Med.*, 12(2):47-53 (1999) ("Nikander"); and Tiano, S.L., UMI Dissertation Services, 1995, Chapter IV, pages 60-68 ("Tiano"). These disclosures teach *away* from formulating an aerosol composition of poorly water soluble active agents.

For example, the art provides that the delivery efficiency of poorly soluble active agents via aerosolization can be unpredictable and inefficient. Cameron teach that nebulization of the water-insoluble drug budesonide showed that minimal amounts of drug substance were aerosolized in vitro. Cameron at 868. Further, studies by Tiano have shown that nebulization of drug particles in the range of one to six microns (1000 to 6000 nm) in diameter, which are contained within the aerosolized water droplets, is very inefficient for air-jet nebulizers and essentially impossible for ultrasonic nebulizers. Tiano at 65, 68 ("It was concluded that an ultrasonic nebulizer could not efficiently aerosolize a respiratory suspension since only the solvent and not the insoluble particles (representing drug) would potentially be delivered to a patient." and "for both [air-jet and ultrasonic] nebulizers . . . the majority of spheres (85-100%) in the original suspension did not leave the nebulizer."). Similar behavior was observed for actual drug suspensions by Nikander.

Therefore, James and Liversidge do not render claims 28-40, 42-45 and 47-59 obvious because there is no motivation to combine these references and there is no reasonable expectation that the combination would be successful.

B.. Rejection of Claims 28-40, 42-45 and 47-59 Under 35 U.S.C. § 103(a) over Wiedmann, Wood and Liversidge

Claims 28-40, 42-45 and 47-59 were rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Wiedmann, Wood and Liversidge.

1. The Examiner's Basis for the Rejection

The examiner stated that Wiedmann teaches a particle size of less than 400 nm, Wood teaches a method of treating a mammal comprising delivering nanoparticles to the lungs of the mammal, and Liversidge teaches that commercial airjet milling techniques provides particles ranging in average particle size from 1000 to 50000 nm. Final Office Action dated

June 17, 2004 at 10. The examiner concluded that "[i]t would have been obvious to one skilled in the art to prepare additional beneficial composition[s] for the delivery and/or treatment of [the] respiratory system by using the composition of the crystalline drug such as steroid containing particles of size less than 1000 nm because surface modifiers, droplets and crystalline particles of less than 1000 nm." *Id.*

2. Wiedmann and Wood Are Not Available As Prior Art

The effective filing date of the present application is February 24, 1995. Commonly assigned Wiedmann was published on May 5, 1998 and was also filed on February 24, 1995. Similarly, Wood was published on July 24, 2001 and claims priority to an application filed on February 24, 1995.

Despite appellants' arguments throughout prosecution of the presently appealed case, the PTO has repeatedly denied appellants' claim to the benefit of domestic priority for an alleged want of written description in U.S. Serial No. 08/394,103 ("the '103 application"). Final Office Action dated June 17, 2004, at 3. However, appellants submitted in two responses (February 4, 2004 and July 22, 2004) a detailed chart analyzing the elements in claims 28-40, 42-45, and 47-59 and indicated where support in the priority '103 application could be found. The claim chart for independent claim 28 is provided in section V above. The claim chart for dependent claims 29-40, 42-45 and 47-59 is set forth in appellants July 22nd response and is reproduced in APPENDIX B.

Accordingly, the subject matter of claims 28-40, 42-45 and 47-49 is fully supported in appellants' priority document. The appealed application complies with the strictures of the written description requirement under 35 U.S.C. § 112, first paragraph, and should enjoy the benefit of the claim to priority. Wiedmann and Wood should therefore be removed as prior art against the present application.

3. Liversidge Alone Does Not Render The Claimed Invention Obvious

As provided above, Liversidge does not disclose aerosolizing nanoparticulate active agent compositions or methods of administering the same. Since Wiedmann and Wood are

not available as prior art, and Liversidge does not teach or suggest the claimed invention, it would not have been obvious for a skilled artisan to arrive at the claimed invention in view of the cited publications.

4. The Examiner Failed To Base The Ultimate Determination Of Patentability On The Entire Record, By A Preponderance Of Evidence, With Due Consideration To The Persuasiveness Of Any Arguments And Any Secondary Evidence

According to U.S. Patent and Trademark Office practice, an examiner must consider any evidence supporting patentability, whether that evidence is found in the specification or is submitted by the appellant. Thus, a decision to maintain a rejection must itself be grounded on the totality of the evidence.

In responding to Appellants' paper dated July 21, 2003, in which Appellants bolstered their support of patentability based on the Cameron, Tiano and Nikander references, the Examiner effectively dismissed that evidence by stating that, "the arguments made about the teachings of Cameron et al., Nikander et al., and Tiano are irrelevant as Wiedmann is still considered prior art." Office Action dated January 21, 2004, at 5. Continuing, the examiner stated that there is motivation to arrive at the claimed invention "because of the combined teachings of Wiedmann et al. and Liversidge et al." but did not explain what that motivation was and dismissed the references that teach away from the combination. *Id.* The Examiner cited no other reference except for Holthuis, already of record, to support his position regarding "the majority" indication in the art.

Accordingly, the examiner did not consider the *totality of the evidence* in maintaining the obviousness rejection and, thus, the Examiner has not established a *prima facie* case of obviousness.

* * *

Because the cited references do not teach or suggest, either alone or in combination the claimed invention, it is courteously requested that the Board reverse the examiner's rejections of the claims.

VIII. EVIDENCE

Copies of any evidence entered and relied upon in the appeal is submitted herewith in an appendix. In particular, Cameron *et al.*, *Crit. Care Med.*, 18(8):866-870 (1990); Nikander *et al., J. Aerosol Med.*, 12(2):47-53 (1999); and Tiano, S.L., UMI Dissertation Services, Chapter IV, pages 60-68 (1995), are provided in APPENDIX C.

IX. CONCLUSION

The Board is respectfully requested to reconsider and reverse the outstanding rejections.

Respectfully submitted,

Date: Dec 17, 2001

By: _____

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APPENDIX A: CLAIMS ON APPEAL

28. A method of delivering an aerosol to the lungs of a mammal comprising the steps of:

(a) providing an aerosol composition, wherein said composition comprises aqueous droplets having a particle size of less than about fifty microns in diameter, wherein the aqueous droplets comprise:

(i) water,

(ii) crystalline particles of a therapeutic agent which is poorly soluble in water, wherein the crystalline particles have a submicron particle size; and

(iii) at least one surface modifier adsorbed on the surface of the crystalline therapeutic agent particles; and

(b) administering said aerosol composition to the respiratory system of said mammal.

29. The method of claim 28, wherein the crystalline particles of a poorly soluble therapeutic agent have an average particle size of less than about 400 nm.

30. The method of claim 29, wherein the crystalline particles of a poorly soluble therapeutic agent have an average particle size of less than about 300 nm.

31. The method of claim 30, wherein the crystalline particles of a poorly soluble therapeutic agent have an average particles size of less than about 100 nm.

32. The method of claim 28, wherein the surface modifier is selected from the group consisting of gelatin, casein, gum acacia, cholesterol, tragacanth, stearic acid, benzalkonium chloride, calcium stearate, glycerol monostearate, cetostearyl alcohol, cetomacrogol emulsifying wax, sorbitan esters, polyoxyethylene alkyl ethers, polyoxyethylene castor oil derivatives, polyethylene glycols, polyoxyethylene stearates, colloidal silicon dioxide, phosphates, sodium dodecylsulfate, carboxymethylcellulose calcium, carboxymethylcellulose sodium, methylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose phthalate, noncrystalline cellulose, magnesium aluminum

silicate, triethanolamine, polyvinyl alcohol, polyvinylpyrrolidone, tyloxapol, a polymer, a polyoxamine, dextran, lecithin, a dialkylester of sodium sulfosuccinic acid, sodium lauryl sulfate, an alkyl aryl polyether sulfonate, a polyoxyethylene sorbitan fatty acid ester, a mixture of sucrose stearate and sucrose distearate, $C_{18}H_{37}CH_2(CON_9CH_3)CH_2(CHOH)_4(CH2)H)_2$, a sulfated block copolymer of ethylene oxide and propylene oxide, and a triblock copolymer of the structure - (PEO) (PBO) (PEO) - having a molecular weight of about 3800 to about 5000.

33. The method of claim 28 comprising at least two surface modifiers.

34. The method of claim 28, wherein the surface modifier is present at an amount of from about 0.1% to about 90% (w/w), based upon the total weight of the combined therapeutic agent and surface modifier.

35. The method of claim 34, wherein the surface modifier is present at an amount of from about 1% to about 75% (w/w), based upon the total weight of the combined therapeutic agent and surface modifier.

36. The method of claim 35, wherein the surface modifier is present at an amount of from about 20% to about 60% (w/w), based upon the total weight of the combined therapeutic agent and surface modifier.

37. The method of claim 28, wherein the therapeutic agent is selected from the group consisting of analgesics, anti-inflammatory agents, anthelminteics, anti-arrhythmic agents, antibiotics, anticoagulants, antidepressants, antidiabetic agents, antiepileptics, antihistamines, antihypertensive agents, antimuscarinic agents, antimycobacterial agents, antineoplastic agents, immunosuppressants, antithyroid agents, antiviral agents, anxiolytic sedatives, astringents, beta-adrenoceptor blocking agents, blood products and substitutes, cardiac inotropic agents, corticosteroids, cough suppressants, diuretics, dopaminergics, haemostatics, immunological agents, lipid regulating agents, muscle relaxants, parasympathomimetics, parathyroid calcitonin and biphosphonates, prostaglandins, radio-pharmaceuticals, sex hormones, anti-allergic agents, stimulants, anorectics, sympathomimetics, thyroid agents, vasodilators, and xanthines.

38. The method of claim 28, wherein the therapeutic agent is beclomethasone dipropionate.

39. The method of claim 28, wherein the therapeutic agent is present in the aqueous medium at an amount of from about 0.1% to about 60% (w/w), based on the total weight of the therapeutic agent and surface modifier.

40. The method of claim 39, wherein the therapeutic agent is present in the aqueous medium at an amount of from about 5% to about 30% (w/w), based on the total weight of the therapeutic agent and surface modifier.

42. The method of claim 28, wherein a jet nebulizer is used to form the aerosol.

43. The method of claim 28, wherein an ultrasonic nebulizer is used to form the aerosol.

44. The method of claim 28, wherein a respiratory illness is treated, which is selected from the group consisting of asthma, emphysema, respiratory distress syndrome, chronic bronchitis, cystic fibrosis, acquired immune deficiency syndrome (AIDS), and AIDS-related pneumonia.

45. The method of claim 28, wherein the aerosol further comprises a liquid propellant.

51. The method of claim 28, wherein at least 90% of the crystalline particles of a poorly soluble therapeutic agent have a particle size of less than about 400 nm.

52. The method of claim 28, wherein at least 95% of the crystalline particles of a poorly soluble therapeutic agent have a particle size of less than about 400 nm.

53. The method of claim 28, wherein at least 99% of the crystalline particles of a poorly soluble therapeutic agent have a particle size of less than about 400 nm.

54. The method of claim 28, wherein at least 90% of the crystalline particles of a poorly soluble therapeutic agent have a particle size of less than about 300 nm.

55. The method of claim 28, wherein at least 95% of the crystalline particles of a poorly soluble therapeutic agent have a particle size of less than about 300 nm.

56. The method of claim 28, wherein at least 99% of the crystalline particles of a poorly soluble therapeutic agent have a particle size of less than about 300 nm.

57. The method of claim 28, wherein at least 90% of the crystalline particles of a poorly soluble therapeutic agent have a particle size of less than about 100 nm.

58. The method of claim 28, wherein at least 95% of the crystalline particles of a poorly soluble therapeutic agent have a particle size of less than about 100 nm.

59. The method of claim 28, wherein at least 99% of the crystalline particles of a poorly soluble therapeutic agent have a particle size of less than about 100 nm.

APPENDIX B: CLAIM CHART

Applicants present the following chart showing explicit support in the '103 application for the dependent claims:

Claim	Exemplary Support in '103 Application
29-31	"the particles have a weight average particle size of less than about 400 nm . . ."; "less than about 300 nm . . ."; "less than about 100 nm . . ." (Page 22, lines 26-35)
32	"Representative examples of surface modifiers include gelatin . . ." (Page 8, line 13 through page 13, line 6)
33	"Two or more surface modifiers can be used in combination." (Page 10, lines 26-27)
34-36	"The concentration of the surface modifier can vary from about 0.1 to about 90%, and preferably is 1-75%, more preferably 20-60%, by weight based on the total combined weight of the therapeutic agent or diagnostic agent and surface modifier." (Page 14, lines 3-9).
37	"Suitable therapeutic or diagnostic agents can be selected from a variety of known classes of therapeutic or diagnostic agents including, for example, analgesics . . ." (Page 6, line 10 through page 8, line 5)
38	"Example 1 . . . Beclomethasone dipropionate . . ." (Page 25, line 11 *et seq.*)
39, 40	"The concentration of the therapeutic agent or diagnostic agent in the liquid medium can vary from about 0.1-60%, and preferably is from 5-30% (w/w)." (Page 13, line 33 through page 14, line 1)
42	"Compressor driven nebulizers incorporate jet technology and use compressed air to generate the aerosol." (Page 5, lines 8-10)
43	"Ultrasonic nebulizers deliver high medication output . . ." (Page 5, lines 16-17).
44	"The aerosols of the present invention are particularly useful in the treatment of respiratory related illnesses such as asthmas, emphysema, respiratoy distress syndrome, chronic bronchitis, cystic fibrosis and acquired immune deficiency syndrome including AIDs related pneumonia." (Page 4, lines 22-27)
45	"liquid propellant containing the nanoparticulate dispersion is released . . ." (Page 5, lines 1-2)
51	"at least 90% of the particles have a weight average particle size of less than about 400 nm . . ." (Page 22, lines28-30)
52	"at least 95% . . . of the particles have a particle size less than the effective average . . ." (Page 23, lines 1-3)
53	"at least 99% of the particles have a particle size less than the effective average . . ." (Page 23, lines 1-3)
54	"the effective average particle size is less than about 300 nm . . ." (Page 22, lines 31-32)
55	"at least 95% . . . of the particles have a particle size less than the effective average . . ." (Page 23, lines 1-3)

Claim	Exemplary Support in '103 Application
56	"at least 99% of the particles have a particle size less than the effective average . . ." (Page 23, lines 1-3)
57	"an effective average particle size of less than about 100 nm has been achieved." (Page 22, lines 33-35)
58	"at least 95% . . . of the particles have a particle size less than the effective average . . ." (Page 23, lines 1-3)
59	"at least 99% of the particles have a particle size less than the effective average . . ." (Page 23, lines 1-3)